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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,495	12/05/2003	Richard B. Borgens	3220-73828	2575

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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,495	BORGENS ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-22,24-26 and 28-32* is/are pending in the application.

4a) Of the above claim(s) *25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,24,28,29,31 and 32* is/are rejected.

7)☒ Claim(s) *19-22 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment and response filed by applicants dated Sept. 21, 2006 have been entered and considered carefully.

Claims 1-17, 23 and 27 have been canceled. Claims 18-26 and newly added claims 28-32 are pending.

Claims 25-26 being drawn to the non-elected claims stayed withdrawn from consideration. Cancellation is recommended.

2. Claims 18, 24, 28-29, 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to employing solvates of an active compound for the treatment of injured nerve tissue. A survey of the specification the term solvate has be associated with the compounds, their salts and "solvates" thereof. Nowhere in the specification described what solvents will be solvated or provided any solvate with any solvents.

Such disclosure provides insufficient description as well as enablement for the claimed scope of "all solvates". The specification contains none of the compound , which is a solvate. While a pharmaceutical addition salt can be prepared routinely upon in possession of an acid or basic compound, the solvate formation is the innate nature of a compound upon contacting certain solvent. Without any description of what solvent will form solvate with which compound and completely silent of the existence of any solvate, the specification offered mere language rather than possession or enablement of the solvates and the process of the disclosure failed to provided any enablement for a solvate which must also have nerve restoration activity.

3. Claims 28-29, 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The scope of claims 28-29, 31-32 not encompassed by claim 30 lack description and antecedent basis in the specification and is considered being drawn to NEW MATTER. The is no description to the all N-4-pyridinyl carbamates will have spinal cord injury restoration activity nor was there any description as to "what" such N-pyridinyl carbamates are beyond the four compounds of claim 30. As a matter of fact, the specification disclosed that all substituted 4-aminopyridines are not analogous in so far as spinal cord injury restoration is concerned. The six compounds disclosed on pages 33-34 all failed to provide such activity. The specification is lacking any description as to "what" other N-(4-pyridinyl) carbamates other than the four disclosed on page 15 would be expected to have such activity.

In addition, it was evidenced in the specification that the methyl carbamate and ethyl carbamate to "behave similarly to 4-AP" (see p.34 middle of the page). Therefore, there is no antecedent basis as to the newly claimed scope that the method operates at a "lower than therapeutic dose of 4-AP", nor how such dosage was measured. Please note that the disadvantage of 4-AP is that the effective dose is also the toxic dose, thus, the drug cannot be used at the effective dose without toxicity. The finding of that four carbamates of page 15 have lower toxicity thus renders the operability in the effective dose range for the four compounds i.e. no toxicity, does not support a claimed to a "lower" than therapeutic dose of 4-AP. No description of such concept was found in the specification, thus, the claims are drawn to NEW MATTER.

Removal of all new matter is required. In re Russmussen 210 USPQ 325.

4. Claims 18, 24, 28-29, 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id.* An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id.* at 740, *Id.* at 1407. The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

The analysis is applied to the instant case.

Nature of invention

The claimed invention is a method of employing all N-(4-pyridyl)carbamates or any solvates to restore action potential or nerve impulse conduction through a mammalian nerve tissue at a lower than therapeutic dose of 4-AP. The finding of insufficient description has been delineated supra.

The state of the art and predictability

The specification provided factual evidence that derivatives of 4-AP employing conventional prodrug concept are highly unpredictable. All six derivatives of 4-AP delineated on pages 33-34 *failed to produce any enhancement* in the recovery CAP amplitude, thus, cannot function at a therapeutic dose without toxicity. Only carbamates disclosed on page 15 tested with similar to 4-AP producing recovery of CAP conduction at a concentration of approximately 100 μM in absence of toxicity. Thus, the high degree of unpredictability has been explicitly described in the specification.

The amount of guidance and working examples

In absence of any other testing results with such high degree of unpredictability evidence by the specification, one must be in possession of the compound and carrying out the same testing as the specification to be able to make any assessment as to the operability of the method. Absent of sufficient data embracing at least one member of each Markush element, there is insufficient enabling support for the now claimed scope in operating the method with unlimited N-(4-pyridyl) carbamates.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 28-29, 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Debay et al. US 3,428,642 supplemented with CA 69:106565 in view of CA 95:58741 and CA 81:9924 supplemented with CA 143:254331.

Determination of the scope and content of the prior art (MPEP §2141.01)

Debay et al. '642 disclosed N-(4-pyridyl)carbamates for which the structural delineation is supplemented by CA 69. The compounds have neuroleptic activity.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and prior art is that the spinal cord conductivity of the prior art compound was not tested or provided. Demenge et al. CA 95 disclosed that the spinal cord have receptor sites for which neuroleptics will have binding activity. Kano et al. disclosed that such neuroleptic binding is electrophysiological in nature. Liu et al. although is a later dated reference provided factual evidence in line with the teaching of the conventional art that neuroleptics evoke electrophysiological binding in spinal cord in similar manner as 4-AP.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of the above references would expect the N-(pyridyl)carbamates of Debay et al. '642 to evoke electrophysiological binding in spinal cord in similar manner as 4-AP because such neuroleptics are expected to operate in analogous manner as that of 4-AP. Especially, although the specification did not disclosed the compounds of Debay et al. '642, claims 28-29, 31-32 embraced such compounds to be operable with or without testing data.

6. The amendment necessitated the new grounds of rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

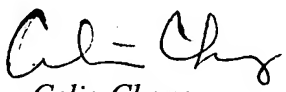
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Claims 19-22, 30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and free from any 112 issues.

.8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie, Ph. D., can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



OACS/Chang
Dec. 7, 2006

Celia Chang
Primary Examiner
Art Unit 1625